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Numerical simulation of osteocyte cell in response to directional mechanical loadings and mechanotransduction analysis: Considering lacunar–canalicular interstitial fluid flow

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ABSTRACT

The osteocyte cell is a bone cell that also functions as a bone mechanosensor. In this work, a three-dimensional (3D) fluid–structure interaction (FSI) model of an osteocyte cell under different mechanical loading conditions was used to obtain a better understanding of osteocyte cell behavior under different physiological conditions. In the current study, both fluid and solid parts of osteocyte cell were considered in order to allow for more accurate results. Five different loading conditions have been applied to the osteocyte cell, and consequently the different interstitial fluid flow velocities and shear stresses have been investigated. Furthermore, using a mathematical model, the change in the stimulus function value with shear stress and NO enzyme was revealed. This work suggests that changes in osteocyte morphology and direction of loadings affect cell stimulation. It was found that cell is mostly stimulated and expanded in the direction experiencing the most shear stress. Finally, the amount of cell stimulation was shown quantitatively and there was strong dependency between stimulus function, shear stress, calcium, and NO concentration.

1. Introduction

Bone is a dynamic tissue that is continuously undergoing modeling and remodeling to meet its mechanical needs according to Wolff's law [1]. Bone remodeling is performed by three types of cells named osteoblasts, osteoclasts, and osteocytes. Osteoblasts lay down new bone, osteoclasts resorb bone, and osteocytes send signals of bone remodeling or resorption to other bone cells. Osteocytes are the most abundant cells among these three types of cells that constitute 90–95% of all bone cells (Fig. 1) [2-3].

Mechanotransduction, a process of converting a biophysical force into a cellular response, is an essential mechanism for a wide variety of physiological functions that allows living organisms to respond to the mechanical changes in their environments [4]. When the bone is subjected to mechanical loading, osteocytes are thought to be able to sense the shear stress induced by interstitial fluid flow in the lacunar–canalicular network, transduce the mechanical signals into biochemical signals, and regulate bone remodeling by affecting effector cells (e.g. other osteocytes, osteoblasts, and osteoclasts) [5,6].

Fluid flow in the osteocytic network of lacunae–canaliculi is one of the physiological mechanical stimuli that osteocytes

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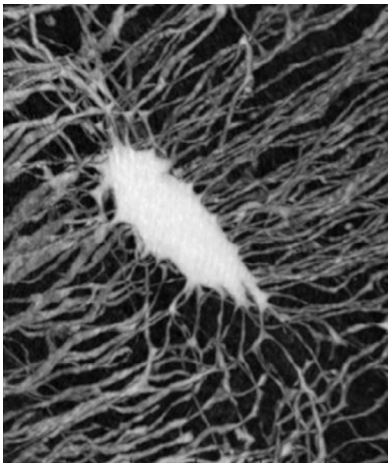

Fig. 1 – High magnification osteocytes embedded within their matrix [2].

respond to in vivo [7]. Physical activities such as walking or jogging also cause interstitial fluid in osteocytes to flow [8].

Weinbaum et al. [9] developed a model for predicting the amount of fluid shear stress (0.8–3 Pa) induced by fluid flow on the membranes of osteocyte processes, which is caused by physiological loading. Klein-Nulend et al. [3] observed that mechanical loading on bone causes the fluid in the lacunar–canalicular system to flow. Osteocyte stimulation produces the factors that regulate bone metabolism. Anderson et al. [10] simulated the fluid domain of an ideal cell and predicted that high shear stresses occur mostly in the canaliculi rather than in the cell body. Furthermore, Rath Bonivtch et al. [11] numerically showed that increasing both the diameter of the cell and elastic modulus of lacuna increases strains. Anderson and Knothe Tate [12] observed that involving more realistic geometry in numerical models leads to an increase of shear stress on the cell processes. Kamioka et al. [13] predicted that geometry of pericellular space greatly affects the fluid velocity around the cell processes. Verbruggen et al. [14,15] showed that velocity, shear stress, and strain in real osteocyte cells are more than those predicted by ideal ones. Although physiological levels of strains are too low (below 0.1% [16] to stimulate osteocytes), Nicolella et al. [17] experimentally measured bone matrix strains around osteocyte lacunae, using a digital image correlation strain measurement technique, and showed that they are considerably greater than macroscopic strain and can reach over 30,000 microstrain. Verbruggen et al. [18] numerically verified the importance of predicted strain amplification in osteocytes by showing that the maximum strains in healthy osteocytes in situ of ~31,000 με are greater than the applied loading of 3000 με.

Wang et al. [19] analyzed the osteocyte cell responses to static and cyclic loads and predicted the strain distribution in these cells by the 3D FE model. Vaughan et al. [20] numerically simulated primary cilia in an osteocyte cell and showed that they might play a role in mediating bone mechanotransduction. Varga et al. [21] used imaging technique to study strains experienced by osteocytes with real geometry under different loading conditions and showed that osteocyte cells experienced different strain values under different loadings directions.

The purpose of this study is to use numerical methods in order to obtain a more accurate and comprehensive analysis to predict the behavior of osteocyte cells under physiological conditions. The influence of external loadings in different directions, effects of the cell body shape and ECM projections were taken into account. Moreover, the shear stress and NO enzyme secretion were quantitatively analyzed. The synergy from these two studies revealed a comprehensive analysis of osteocyte cells.

2. Materials and methods

2.1. FSI model

2.1.1. Geometry

The geometry was formed from a body, the cell processes, the interstitial fluid, and the extracellular matrix that covers all parts of the cell. The cell body and the pericellular space around the cell body (lacunae) were plotted as an ellipsoid. Major and minor axes of the elliptical cell body were equal to 13.5 and 7.5 μm, while the thickness of the pericellular space around the cell body was 0.75 μm. The process with a diameter of 0.6 μm was also plotted, and the fluid domain around the process was created by offsetting 0.1 μm from the process in which the interstitial fluid flows. Finally, the entire cell was placed inside a cube, called the extracellular matrix (ECM) (Fig. 2(a) and (b)) [14]. The interstitial fluid fills the space between the cell and the ECM.

The ECM projections inside the canaliculi were considered; the projections were 0.02 μm away from the process wall and 1 μm from each other.

Three different cell body shapes were considered: scalene ellipsoid with a major to minor axis ratio of 5/3, prolate ellipsoid with major to minor axis ratio of 4/3, and a spherical configuration.

Various models of the osteocyte cell were meshed via ANSYS software, and 353748 and 152169 linear tetrahedral elements were used for solid and fluid parts of the geometry, respectively.

2.1.2. Material properties

The elastic modulus of 16 GPa and Poisson's ratio of 0.38, respectively, were used for the ECM [22] and an elastic modulus and Poisson's ratio of 4.47 KPa and 0.3, respectively, were chosen for the cell body and processes [23]. A density of 997 Kgm^{-3} and dynamic viscosity of 0.000855 $kgm^{-1}s^{-1}$ [10] were considered for the interstitial fluid. It should also be noted that all solid materials have been modeled as linear elastic and isotropic.

2.1.3. Boundary conditions and loadings

The FSI model consists of three parts: analyzing the fluid and solid interaction in the osteocyte cell without ECM projections, then studying the effects of projections inside the canaliculi, and investigating the effects of different cell body shapes.

In a two-way FSI modeling, the solutions of the CFD analysis are mapped onto the solid domain and subsequently CFD received the displacements from solid domain. So, the fluid and solid domains are coupled by passing loads across